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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/829,936	04/11/2001	Emmanuel Conseiller	ST98033	7710

29693 7590 07/18/2003

WILEY, REIN & FIELDING, LLP
ATTN: PATENT ADMINISTRATION
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EXAMINER	
HUFF, SHEELA JITENDRA	
ART UNIT	**PAPER NUMBER**
1642	21

DATE MAILED: 07/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/829,936	CONSEILLER ET AL.	
	Examiner	Art Unit	
	Sheela J Huff	1642	

-- The MAILING DATE of this communication appears on the c ver sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-97* is/are pending in the application.

4a) Of the above claim(s) *32-97* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31 and 33 (as they read on SEQ ID NO. 22)* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group IV, claims 31 and 33 (SEQ ID NO. 22) in Paper No. 19 is acknowledged. The traversal is on the ground(s) that each sequence shares the same functional interaction and that the PTO rules states that up to 10 sequences will be examined. This is not found persuasive because each polypeptide is has a distinct chemical and structural make-up and due the complexity of the art and the enormous size of the databases, searching all the sequences present in the instant application would constitute an undue burden on the Office. Thus this constitutes an "exceptional" case.

The requirement is still deemed proper and is therefore made FINAL.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in France on 10/12/98. It is noted, however, that applicant has not filed a certified copy of the French application as required by 35 U.S.C. 119(b).

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
It does not mention PCT/FR99/02465.

Claim Rej ctions - 35 USC § 112

Claim 31 and 33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO. 22, does not reasonably provide enablement for any and all polypeptides, either whole or in part, capable of "interacting specification with oncogenic forms of p53, and capable of stimulating cell growth, and capable of blocking the antiproliferative effects of the wild-type form of p53". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims..

The claim is drawn to polypeptides capable of "interacting specification with oncogenic forms of p53, and capable of stimulating cell growth, and capable of blocking the antiproliferative effects of the wild-type form of p53". While the specification does disclose several different sequences, the specification does not disclose the general characteristics required for a sequence possessing the claimed characteristics. In other words, there is no guidance as to specific domains required for interaction, blocking or stimulation. Applicant has not demonstrated that there are common domains in fibulin-2 and mpb1 which are responsible for these interactions. Thus, once skilled in the art would not know which polypeptides may possess the claimed activities. Furthermore, applicant is claiming that "part of" the polypeptide can possess the claimed activities. Applicant has not demonstrated which "part" of the polypeptide possess this activity. These polypeptides comprise over 400 amino acids

and it is not clear if a linear of sequence is needed or if a certain conformation of the "part" of the peptide must be adopted before the peptide can possess the claimed activities. One of ordinary skill in the art would be faced with undue burden to test the multitude of polypeptides to determine which of them, or which "part", possessed the claimed characteristics.

Claims 31 and 33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to polypeptides having 70-100% identity with SEQ ID no. 22 (see applicant's definition of "derivative on page 11 of the specification). While the amino acid sequence of SEQ ID NO:22 is adequately described in the specification as-filed, thereby providing an adequate basis for the polypeptide of SEQ ID NO:22; there is insufficient written description as to the identity of a polypeptide having at least 70-99% sequence identity to SEQ ID NO:22 that would still maintain the function of the polypeptide. Consequently, the specification does not provide an adequate written description of an antibody to a polypeptide having at least 70-99% sequence identity to SEQ ID NO:22.

The specification as filed does not provide adequate written description support for an antibody to a polypeptide having at least 70-99% sequence identity to SEQ ID NO:22. Polypeptides having diverse functions are encompassed by the phrase 70-99%

identity. Thus a broad genus having potentially highly diverse functions is encompassed by the phrase 70-99% sequence identity" and conception cannot be achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. For example, Skolnick et al. (Trends in Biotech., 18(1):34-39, 2000) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). Adequate written description requires more than a mere statement that it is part of the invention. The sequence itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

Therefore, only SEQ ID No. 22 meets the written description provision of 35 U.S.C. 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claims 31 and 33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO. 22, does not reasonably provide enablement for derivatives of Seq ID No 22. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of proteins broadly encompassed by the claims and the claims broadly encompass a significant number of inoperative species. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and still retain similar biological activity requires a (1) knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e., expectantly intolerant to modification), and (2) detailed knowledge of the ways in which the protein's structure relates to its function. However, the problem of predicting protein structure from mere sequence data of a single protein and in turn utilizing predicted structural determinations

to ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex and well outside the realm of routine experimentation.

1. While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications of other types and the positions within the protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining similar biological activity are limited in any protein. The result of such modifications is unpredictable based on the instant disclosure. One skilled in the art would expect any tolerance to modification shown for a given protein to diminish with each further and additional modification, e.g., multiple substitutions. The sequence of some proteins is highly conserved and one skilled in the art would not expect tolerance to any amino acids modifications in such proteins.

2. The specification does not support the broad scope of the claims which encompass all modifications and fragments because the specification does not disclose the following:

1. The amino acid sequence for the claimed protein;

2. The general tolerance to modification and extent of such tolerance;

3. The specific positions and regions of the sequence(s) which can be predictably modified and which regions are critical;

4. What fragments, if any, can be made which retain the biological activity of the intact protein; and

5. The specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

3. Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed protein in manner reasonable correlated with the scope of the claims broadly including any number of additions, deletions, or substitutions and fragments of any size. The scope of the claims must bear a reasonable correlation with the scope of enablement. See In re Fisher, 166 USPQ 19 24 (CCPA 1970). Without such guidance, the changes which can be made in the protein's structure and still maintain biological activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See Amgen, Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F,2d 1200, 18

USPQ 1016 (Fed. Cir. 1991) at 18 USPQ 1026 1027 and Ex parte Forman, 230 USPQ 546 (BPAI 1986).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 31 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 97/38012.

The polypeptide sequence in Figure 1 of this reference is 99.7% identical to the claimed sequence. Thus, the reference reads on the "derivative" of SEQ ID No. 22. The alignment for the sequences is attached to this action. It is inherent that the polypeptide in the reference is capable of "interacting specification with oncogenic forms of p53, and capable of stimulating cell growth, and capable of blocking the antiproliferative effects of the wild-type form of p53".

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. US 5916769.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheela J Huff whose telephone number is 703-305-7866. The examiner can normally be reached on Tuesday 5:30am-11:30am and Fridays 6:00am-4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Sheela J Huff
Primary Examiner
Art Unit 1642

sjh
July 11, 2003